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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET, SUITE #1600
ONE WORLD TRADE CENTER
PORTLAND, OR 97204-2988

EXAMINER	
DEJONG, ERIC S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,269	KALLIONIEMI ET AL.	
	Examiner	Art Unit	
	Eric S. DeJong	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40 and 64-67* is/are pending in the application.

4a) Of the above claim(s) *15-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 64-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-40 and 64-67* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the invention of Group I (claims 1-40) and election of a computer implemented method of counting nucleic acid probe signals comprising species (B): an unspecified method in the reply filed on 03/04/2005 is acknowledged. The traversal is on the grounds that applicants disagree with the species and subspecies election requirement for Group I and that all species could be properly examined without presenting an undue burden of search.

This is not found persuasive because the generic claims 1-14 are not restricted by the additional limitation of counting visible signals from probes used in *in situ* hybridization of biological of a biological sample comprising obtaining a plurality of images, construction of a three-dimensional model, and counting discrete signals at different levels of the three dimensional model. Therefore, a search performed for the methods presented in generic claims 1-14 is not coextensive with a search performed for methods specifically drawn to methods that, for example, also requires the additional limitation of constructing a three-dimensional model. Since the search including all species and subspecies together would not be coextensive, the requirement is still deemed proper and is therefore made FINAL.

Claims 15-40 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction and election

requirements in the reply filed on 03/04/2005. Claims 41-63 have been canceled. Claims 1-14 and 64-67 are currently under examination.

Claim Rejections - 35 USC § 102

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 10, 11, 13, 14, and 64-66 are rejected under 35 U.S.C. 102(e)(2) as being clearly anticipated by Garini et al. (U.S. Patent No. 5,817,462).

Claims 1, 64, and 65: Garini et al. discloses a spectral imaging method, system and means for simultaneous detection of multiple fluorophores aimed at detecting and analyzing in situ hybridizations employing numerous chromosome paints and loci specific probes (a method for counting nucleic acid probe signals in a region of interest in a biological specimen). See Garini et al., Abstract. The spectral algorithms, processing and visualization techniques are specifically directed toward computer implemented applications and read on the claimed computer-implemented method and computer systems. See Garini et al, at least column 16, lines 38-56 and column 19, line 9 through column 20, line 61. The disclosed method provides for the analysis of multiple cell (defined as " both a biological cell and also a region in the field of view of the instrument") types stained with different fluorophores, wherein an algorithm is applied to analyze a given cell or region for each type of fluorescent signal being used and provide a count of the number of cells or regions pertaining to each fluorophore (in a computer

system, automatically counting a number of test signals from a test probe; in a computer system, automatically counting a number of reference signals from a reference probe; the region of interest comprises multiple cells). See Garini et al., column 19, line 9-48 and column 27, line 33-59. It is further emphasized in Garini et al., column 54, lines 28-40, that the algorithms disclosed and incorporated into the method employ automatic procedures that are well known in the art. Further, Garini et al. discloses the determination of a ratio between multiple frequencies of fluorescence pertaining to different probes hybridized to chromosomes or specific loci (determining a ratio of the automatically-counted test signal from the test probe to the automatically-counted reference signals from the reference probe). See Garini et al., column 9, line 26-35 and column 23, line 18 through column 24, line 8.

Claim 2: Garini et al. discloses the use of centromere specific DNA probes in Example 1, column 37, line 66 through column 38, line 27 (the reference probe is a ploynucleotide that hybridizes to a centromere). Further Garini et al. discloses an embodiment of the invention wherein probe hybridization is directed to chromosomal loci and provides for the detection of a cell nucleus. See Garini et al., column 6, line 66 through column 67, line 42. Example 1 also teaches that duration of exposing a sample to hybridizing probes directly relates to the amount of observable probes signal, and therefore, under a broad interpretation, each measurement of probe signal provides for an approximation of the probe target present in a given sample rather than an absolute measurement of all possible probe targets (the number of reference signals from the reference probe approximates a nucleus count in the biological specimen).

Claim 3: Garini et al. discloses that a fluorescent in situ hybridization method available to the disclosed invention can provide information on the location of the labeled probe, the number of labeled sites on each chromosome, and the intensity of labeling at each site (the reference probe recognizes a target on a same chromosome as the test probe). See Garini et al., column 26, lines 45-58.

Claims 4 and 5: Garini et al. discloses the invention can be used to analyze genes at the chromosome level (the test probe is a polynucleotide that hybridizes to a target sequence in a gene, and the reference probe is a polynucleotide that hybridizes to a reference sequence). See Garini et al., column 25, lines 16-23. Further, it is disclosed that this is an important example of where "the detection of multiple fluorescent probes can be a significant advantage" (the reference probe recognizes the same chromosome on which the gene of interest is contained). See Garini et al., column 25, lines 16 and 17.

Claims 6 and 66: Garini et al. teaches sequentially acquiring images of the emissions of multiple fluorescent probes to address the issue of overlapping signal in probe samples (obtaining a plurality of successive images of the region of interest to distinguish signals in the biological specimen). See Column 23, lines 7-27.

Claims 10 and 11: Garini et al. teaches that the imaging spectrometers used in context of the disclosed invention measure the intensity of light coming from every pixel in the field of view, but also measure the spectrum of each pixel in a predefined wavelength range (a quantity of the test probe signals and reference probe signals are determined). See Garini et al., column 3, lines 46-59 and column 15, lines 44-58.

Claims 13 and 14: Garini et al. provide pictures obtained using the disclosed invention wherein multiple fluorescent probes were hybridized to chromosomes and establish a standard karyotype display without any reference to the boundaries of a cell nucleus or a cell (the ratio of signals is determined without reference to boundaries of a cell nucleus, without reference to the boundaries of a cell). See Garini et al., for example Figures 9A, 9B, 10 and 11.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14 and 64-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garini et al. taken in view of Cabib et al. (U.S. Patent No. 5,784,162).

Garini et al., as discussed above, discloses a spectral imaging method, system and means for simultaneous detection of multiple fluorophores aimed at detecting and analyzing in situ hybridizations employing numerous chromosome paints and loci specific probes. However Garini et al. does not fairly teach the claimed invention wherein successive images are optical sections of the region of interest, are at different depths of the biological specimen, are transformed into digital representations in which contiguous signal segments are combined into a single signal, or are obtained by confocal microscopy.

Garini et al. does teach that the disclosed invention is potentially useful in all applications in which spectral differences exist between chemical constituents whose special distribution and organization within an image are of interest, and that the spectral imaging methods disclosed in Cabib et al. (U.S. Patent No. 5,784,162) can be used to detect such spatial organization in a given sample. See Garini et al., column 5, lines 16-47.

Claims 7 and 8: Cabib et al. disclosed a mapping technique in the context of the disclosed invention that allows for image acquisition by focusing on specific depths within a cell (successive images are optical sections; the optical sections are at different depths of the biological specimen). See Cabib et al., column 38, line 47 through column 39, line 9.

Claim 9: The instant limitation of successive images being transformed into digital representations in which contiguous signal segments in successive optical scans are combined into a single signal in a particular optical section, under a reasonably

broad interpretation, can be read as simply a two-dimensional digital representation of contiguous optical layers. Figure 12 and the related caption found in Cabib et al., column 14, lines 14-31, reads on the broad interpretation instant limitation, as images of multiple levels of fluorescence images taken of a paramecium are presented as well as an overall (combined) fluorescence image of the paramecium. Further, Cabib et al. establish that the disclosed invention embodies images derived from both spectroscopic and digital methods that are well known in the art. See Cabib et al., column 19, lines 28-41.

Claims 12 and 67: Cabib et al. specifically disclose that preferred embodiments the microscope is selected from the group consisting of a reflection microscope, a transmission microscope, a fluorescence microscope, an upright microscope, an inverted microscope, a dark field microscope, a confocal microscope, a standing wave confocal microscope and a reflection contrast microscope (wherein successive images are obtained by confocal microscopy). See Cabib et al., column 7, lines 53-59.

Taken in view of Cabib et al., it would have been obvious to one of skill in the art to employ the spectral imaging method, system and means for simultaneous detection of multiple fluorophores aimed at detecting and analyzing in situ hybridizations employing numerous chromosome paints and loci specific probes as taught by Garini et al., wherein successive images are optical sections of the region of interest, are at different depths of the biological specimen, are transformed into digital representations in which contiguous signal segments are combined into a single signal, or are obtained by confocal microscopy.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 272-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Ardin H. Marschel 4/17/05
ARDIN H. MARSCHEL
PRIMARY EXAMINER